

# SEQUENCE LISTING

<110> CANFIELD, William

<120> HIGHLY PHOSPHORYLATED ACID BETA-GLUCOCEREBROSIDASE AND METHODS OF TREATING GAUCHER'S DISEASE

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725 730 735

Arg Ser Phe Leu Met Asn Ser Gln His Ala Lys Ile Lys Asn Gln Ala  
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Ile Ile Thr Asp Glu Thr Asn Asp Ser Leu Val Ala Pro Gln Glu Lys  
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Asp Gln Gly Gln Asn Pro Pro Leu Asp Leu Glu Thr Thr Ala Arg Phe  
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Arg Val Glu Thr His Thr Gln Lys Thr Ile Gly Gly Asn Val Thr Lys  
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Asn Ile Ser Gln Val Phe Asp Glu Val Asp Thr Asp Gln Ser Gly Val  
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Pro Leu Ser Leu Gln Asp Leu Thr Gly Leu Glu His Met Leu Ile Asn  
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Cys Ser Lys Met Leu Pro Ala Asp Ile Thr Gln Leu Asn Asn Ile Pro  
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Pro Thr Gln Glu Ser Tyr Tyr Asp Pro Asn Leu Pro Pro Val Thr Lys  
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Ser Leu Val Thr Asn Cys Lys Pro Val Thr Asp Lys Ile His Lys Ala  
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Tyr Lys Asp Lys Asn Lys Tyr Arg Phe Glu Ile Met Gly Glu Glu Glu  
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Ile Ala Phe Lys Met Ile Arg Thr Asn Val Ser His Val Val Gly Gln  
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 <400> 12

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Gln Gly Pro Ala Pro Ala Cys Ala Gly Lys Met Lys Val Val Glu Glu  
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Pro Asn Thr Phe Gly Leu Asn Asn Pro Phe Leu Pro Gln Ala Ser Arg  
35 40 45

Leu Gln Pro Lys Arg Glu Pro Ser Ala Val Ser Gly Pro Leu His Leu  
50 55 60

Phe Arg Leu Ala Gly Lys Cys Phe Ser Leu Val Glu Ser Thr Tyr Lys  
65 70 75 80

Tyr Glu Phe Cys Pro Phe His Asn Val Thr Gln His Glu Gln Thr Phe  
85 90 95

Arg Trp Asn Ala Tyr Ser Gly Ile Leu Gly Ile Trp His Glu Trp Glu  
100 105 110

Ile Ile Asn Asn Thr Phe Lys Gly Met Trp Met Thr Asp Gly Asp Ser  
115 120 125

Cys His Ser Arg Ser Arg Gln Ser Lys Val Glu Leu Thr Cys Gly Lys  
130 135 140

Ile Asn Arg Leu Ala His Val Ser Glu Pro Ser Thr Cys Val Tyr Ala  
145 150 155 160

Leu Thr Phe Glu Thr Pro Leu Val Cys His Pro His Ser Leu Leu Val  
165 170 175

Tyr Pro Thr Leu Ser Glu Ala Leu Gln Gln Arg Leu Asp Gln Val Glu  
180 185 190

Gln Asp Leu Ala Asp Glu Leu Ile Thr Pro Gln Gly Tyr Glu Lys Leu  
195 200 205

Leu Arg Val Leu Phe Glu Asp Ala Gly Tyr Leu Lys Val Pro Gly Glu  
210 215 220

Thr His Pro Thr Gln Leu Ala Gly Gly Ser Lys Gly Leu Gly Leu Glu  
225 230 235 240

Thr Leu Asp Asn Cys Arg Lys Ala His Ala Glu Leu Ser Gln Glu Val  
245 250 255

Gln Arg Leu Thr Ser Leu Leu Gln Gln His Gly Ile Pro His Thr Gln  
260 265 270

Pro Thr Glu Thr Thr His Ser Gln His Leu Gly Gln Gln Leu Pro Ile  
275 280 285

Gly Ala Ile Ala Ala Glu His Leu Arg Ser Asp Pro Gly Leu Arg Gly  
290 295 300

Asn Ile Leu  
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<211> 460  
<212> DNA  
<213> Rattus rattus

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taacccccaaa ggtttccccg agctgaacaa gcagaccaag aagaacatga gcatcagtgg 180  
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aatcatgata tcagtagtat tcctctgaaa tggcacacat ttttctaata agaacttgaa 420  
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<211> 113  
<212> PRT  
<213> Rattus rattus

<400> 14

Phe Pro Pro Thr Phe Lys Glu Thr Ser Gln Leu Lys Thr Lys Leu Pro  
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Glu Asn Leu Ser Ser Lys Ile Lys Leu Leu Gln Leu Tyr Ser Glu Ala  
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Ser Val Ala Leu Leu Lys Leu Asn Asn Pro Lys Gly Phe Pro Glu Leu  
 35 40 45

Asn Lys Gln Thr Lys Lys Asn Met Ser Ile Ser Gly Lys Glu Leu Ala  
 50 55 60

Ile Ser Pro Ala Tyr Leu Leu Trp Asp Leu Ser Ala Ile Ser Gln Ser  
 65 70 75 80

Lys Gln Asp Glu Asp Val Ser Ala Ser Arg Phe Glu Asp Asn Glu Glu  
 85 90 95

Leu Arg Tyr Ser Leu Arg Ser Ile Glu Arg His Asp Ser Met Ser Pro  
 100 105 110

Leu

<210> 15  
 <211> 1105  
 <212> DNA  
 <213> Drosophila melanogaster

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 <212> PRT  
 <213> Drosophila melanogaster

<400> 16

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Asn Gly Gln Ile Pro Ser Trp Leu Asp Leu Ser Tyr Glu Arg Val Thr  
35 40 45

Val Val Pro His Glu Val Leu Ala Pro Asp Pro Asp Gln Leu Pro Thr  
50 55 60

Phe Ser Ser Ser Ala Ile Glu Thr Phe Leu His Arg Ile Pro Lys Leu  
65 70 75 80

Ser Lys Arg Phe Leu Tyr Leu Asn Asp Asp Ile Phe Leu Gly Ala Pro  
85 90 95

Leu Tyr Pro Glu Asp Leu Tyr Thr Glu Ala Glu Gly Val Arg Val Tyr  
100 105 110

Gln Ala Trp Met Val Pro Gly Cys Ala Leu Asp Cys Pro Trp Thr Tyr  
115 120 125

Ile Gly Asp Gly Ala Cys Asp Arg His Cys Asn Ile Asp Ala Cys Gln  
130 135 140

Phe Asp Gly Gly Asp Cys Ser Glu Thr Gly Pro Ala Ser Asp Ala His  
145 150 155 160

Val Ile Pro Pro Ser Lys Glu Val Leu Glu Val Gln Pro Ala Ala Val  
165 170 175

Pro Gln Ser Arg Val His Arg Phe Pro Gln Met Gly Leu Gln Lys Leu  
180 185 190

Phe Arg Arg Ser Ser Ala Asn Phe Lys Asp Val Met Arg His Arg Asn  
195 200 205

Val Ser Thr Leu Lys Glu Leu Arg Arg Ile Val Glu Arg Phe Asn Lys  
210 215 220

Ala Lys Leu Met Ser Leu Asn Pro Glu Leu Glu Thr Ser Ser Ser Glu  
225 230 235 240

Pro Gln Thr Thr Gln Arg His Gly Leu Arg Lys Glu Asp Phe Lys Ser  
245 250 255

Ser Thr Asp Ile Tyr Ser His Ser Leu Ile Ala Thr Asn Met Leu Leu  
260 265 270

Asn Arg Ala Tyr Gly Phe Lys Ala Arg His Val Leu Ala His Val Gly  
275 280 285

Phe Leu Ile Asp Lys Asp Ile Val Glu Ala Met Gln Arg Arg Phe His  
290 295 300

Gln Gln Ile Leu Asp Thr Ala His Gln Arg Phe Arg Ala Pro Thr Asp  
305 310 315 320

Leu Gln Tyr Ala Phe Ala Tyr Tyr Ser Phe Leu Met Ser Glu Thr Lys  
325 330 335

Val Met Ser Val Glu Glu Ile Phe Asp Glu Phe Asp Thr Asp Gly Ser  
340 345 350

Ala Thr Trp Ser Asp Arg Glu Val Arg Thr Phe Leu Thr Arg Ile Tyr  
355 360 365

Gln Pro Pro Leu Asp Trp Ser Ala Met Arg Tyr Phe Glu Glu Val Val  
370 375 380

Gln Asn Cys Thr Arg Asn Leu Gly Met His Leu Lys Val Asp Thr Val  
385 390 395 400

Glu His Ser Thr Leu Val Tyr Glu Arg Tyr Glu Asp Ser Asn Leu Pro  
405 410 415

Thr Ile Thr Arg Asp Leu Val Val Arg Cys Pro Leu Leu Ala Glu Ala  
420 425 430

Leu Ala Ala Asn Phe Ala Val Arg Pro Lys Tyr Asn Phe His Val Ser  
435 440 445

Pro Lys Arg Thr Ser His Ser Asn Phe Met Met Leu Thr Ser Asn Leu  
 450 455 460

Thr Glu Val Val Glu Ser Leu Asp Arg Leu Arg Arg Asn Pro Arg Lys  
 465 470 475 480

Phe Asn Cys Ile Asn Asp Asn Leu Asp Ala Asn Arg Gly Glu Asp Asn  
 485 490 495

Glu Asp Gly Ala Pro Ser  
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<210> 17  
 <211> 2183  
 <212> DNA  
 <213> Homo sapiens

<400> 17  
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<210> 18  
<211> 515  
<212> PRT  
<213> Homo sapiens

<400> 18

Met Ala Thr Ser Thr Gly Arg Trp Leu Leu Leu Arg Leu Ala Leu Phe  
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Gly Phe Leu Trp Glu Ala Ser Gly Gly Leu Asp Ser Gly Ala Ser Arg  
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Asp Asp Asp Leu Leu Leu Pro Tyr Pro Arg Ala Arg Ala Arg Leu Pro

35	40	45																	
Arg	Asp	Cys	Thr	Arg	Val	Arg	Ala	Gly	Asn	Arg	Glu	His	Glu	Ser	Trp				
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Pro	Pro	Pro	Pro	Ala	Thr	Pro	Gly	Ala	Gly	Gly	Leu	Ala	Val	Arg	Thr				
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Phe	Val	Ser	His	Phe	Arg	Asp	Arg	Ala	Val	Ala	Gly	His	Leu	Thr	Arg				
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Ala	Val	Glu	Pro	Leu	Arg	Thr	Phe	Ser	Val	Leu	Glu	Pro	Gly	Gly	Pro				
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Gly	Gly	Cys	Ala	Ala	Arg	Arg	Arg	Ala	Thr	Val	Glu	Glu	Thr	Ala	Arg				
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Thr	Leu	Val	Thr	Gly	Tyr	Leu	Ser	Glu	Glu	Glu	Val	Leu	Asp	Thr	Glu				
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Asn	Pro	Phe	Val	Gln	Leu	Leu	Ser	Gly	Val	Val	Trp	Leu	Ile	Arg	Asn				
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Asp	Gly	His	Thr	Glu	Gln	Arg	Gly	Ile	Asn	Leu	Trp	Glu	Met	Ala	Glu				
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Phe Leu Leu Lys Gln Asp Val Val Asn Ala Ile Asn Leu Asp Gly Gly  
275 280 285

Gly Ser Ala Thr Phe Val Leu Asn Gly Thr Leu Ala Ser Tyr Pro Ser  
290 295 300

Asp His Cys Gln Asp Asn Met Trp Arg Cys Pro Arg Gln Val Ser Thr  
305 310 315 320

Val Val Cys Val His Glu Pro Arg Cys Gln Pro Pro Asp Cys His Gly  
325 330 335

His Gly Thr Cys Val Asp Gly His Cys Gln Cys Thr Gly His Phe Trp  
340 345 350

Arg Gly Pro Gly Cys Asp Glu Leu Asp Cys Gly Pro Ser Asn Cys Ser  
355 360 365

Gln His Gly Leu Cys Thr Glu Thr Gly Cys Arg Cys Asp Ala Gly Trp  
370 375 380

Thr Gly Ser Asn Cys Ser Glu Glu Cys Pro Leu Gly Trp His Gly Pro  
385 390 395 400

Gly Cys Gln Arg Arg Cys Lys Cys Glu His His Cys Pro Cys Asp Pro  
405 410 415

Lys Thr Gly Asn Cys Ser Val Ser Arg Val Lys Gln Cys Leu Gln Pro  
420 425 430

Pro Glu Ala Thr Leu Arg Ala Gly Glu Leu Ser Phe Phe Thr Arg Thr  
435 440 445

Ala Trp Leu Ala Leu Thr Leu Ala Leu Ala Phe Leu Leu Leu Ile Ser  
450 455 460

Ile Ala Ala Asn Leu Ser Leu Leu Leu Ser Arg Ala Glu Arg Asn Arg  
465 470 475 480

Arg Leu His Gly Asp Tyr Ala Tyr His Pro Leu Gln Glu Met Asn Gly  
485 490 495



Glu Pro Leu Ala Ala Glu Lys Glu Gln Pro Gly Gly Ala His Asn Pro  
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Phe Lys Asp  
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 <211> 2005  
 <212> DNA  
 <213> Mus musculus

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<210> 20  
 <211> 492  
 <212> PRT  
 <213> Mus musculus  
 <400> 20

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Glu Ser Trp Pro Pro Pro Pro Leu Ala Thr His Glu Pro Arg Ala Pro  
 35 40 45

Ser His His Ala Ala Val Arg Thr Phe Val Ser His Phe Glu Gly Arg  
 50 55 60

Ala Val Ala Gly His Leu Thr Arg Val Ala Asp Pro Leu Arg Thr Phe  
 65 70 75 80

Ser Val Leu Glu Pro Gly Gly Ala Gly Gly Cys Gly Gly Arg Ser Ala  
 85 90 95

Ala Ala Thr Val Glu Asp Thr Ala Val Arg Ala Gly Cys Arg Ile Ala  
100 105 110

Gln Asn Gly Gly Phe Phe Arg Met Ser Thr Gly Glu Cys Leu Gly Asn  
115 120 125

Val Val Ser Asp Gly Arg Leu Val Ser Ser Ser Gly Gly Leu Gln Asn  
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Gly Cys His Cys Asp Ala Gly Trp Thr Gly Ser Asn Cys Ser Glu Glu  
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Cys Pro Leu Gly Trp Tyr Gly Pro Gly Cys Gln Arg Pro Cys Gln Cys  
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<212> DNA

<213> Mus musculus

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<213> Artificial Sequence

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<220>
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<400> 22

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Gly Ser Thr Gly
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<210> 23
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TOEPLITZ

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<211> 2279  
<212> DNA  
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<211> 536
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<213> Homo sapiens

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Arg Val Ser Ile Met Ala Gly Ser Leu Thr Gly Leu Leu Leu Leu Gln
          20          25          30

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```

Ala Val Ser Trp Ala Ser Gly Ala Arg Pro Cys Ile Pro Lys Ser Phe
          35          40          45

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Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser  
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Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu  
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Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln  
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Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln  
100 105 110

Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala  
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Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu  
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Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val  
145 150 155 160

Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp  
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Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp  
180 185 190

Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln  
195 200 205

Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu  
210 215 220

Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro  
225 230 235 240

Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu  
245 250 255

Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu  
260 265 270

Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu

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Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu				
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Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr				
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Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr				
	340		345	350
Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg				
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Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser				
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Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met				
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Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly				
	405		410	415
Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp				
	420		425	430
Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp				
	435		440	445
Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys				
	450		455	460
Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys				
465		470		475 480
Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val				
	485		490	495
Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys				
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His Thr Tyr Leu Trp Arg Arg Gln  
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<210> 26  
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<400> 26

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 35 40 45

Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser  
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Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu  
 65 70 75 80

Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln  
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Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln  
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Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala  
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Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val  
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Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp  
165 170 175

Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp  
180 185 190

Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln  
195 200 205

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210 215 220

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Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu  
260 265 270

Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu  
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Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly  
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Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu  
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Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr  
325 330 335

Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr  
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Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg  
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370 375 380

Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met



385                      390                      395                      400

Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly  
405 . 410 415

Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp  
420 425 430

Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp  
435 440 445

Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys  
450 455 460

Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys  
465 470 475 480

Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val  
485 490 495

Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys  
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Asp Pro Ala Val Gly Phe Leu Glu Thr Ile Ser Pro Gly Tyr Ser Ile  
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His Thr Tyr Leu Trp His Arg Gln  
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Arg Ala Arg Tyr Lys Arg  
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